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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------------|-------------|----------------------|---------------------|-------------------|
| 10/033,621 | 12/27/2001 | Peter C. Meltzer | 70207/56,579 | 9295 |
| 21874 | 7590 | 06/16/2005 | | EXAMINER |
| EDWARDS & ANGELL, LLP | | | | AULAKH, CHARANJIT |
| P.O. BOX 55874 | | | | |
| BOSTON, MA 02205 | | | ART UNIT | PAPER NUMBER |
| | | | 1625 | |

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|---------------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/033,621 | MELTZER ET AL. | |
| | Examiner Charanjit S. Aulakh | Art Unit 1625 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06 April 2005.
2a) This action is FINAL. 2b) This action is non-final.
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-7,9-18,20-31,33-35,37 and 39-49 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-7, 9-18, 20-31, 33-35, 37 and 39-49 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

DETAILED ACTION

1. According to paper filed on April 6, 2005, the applicants have canceled claims 8 and 19; amended claims 1, 5, 6, 9, 12, 16, 17, 24, 44 and 45 and furthermore, have added new claims 46-49.
2. Claims 1-7, 9-18, 20-31, 33-35, 37 and 39-49 are now pending in the application.

Response to Arguments

3. Applicant's arguments filed on April 6, 2005 have been fully considered but they are not persuasive regarding enablement, indefiniteness and most of prior art rejections. In regard to enablement, the examiner does not agree with the applicants arguments that one of ordinary skill in the art can readily determine which conditions can be treated according to methods of the invention. As stated in the previous office actions, there is no teaching either in the specification or prior art that serotonin uptake and/or dopamine uptake inhibitors are either well known to have therapeutic utility in treating every known neurodegenerative disease, psychiatric disease, dopamine dysfunction, cocaine abuse and clinical dysfunctions or efficacious in known animal models of every known neurodegenerative disease, psychiatric disease, dopamine dysfunction, cocaine abuse and clinical dysfunctions.

In regard to indefiniteness rejections, the examiner does not agree with the applicants arguments that claims 25-28 are clear and definite. The applicants did not address the issue of difference between inhibiting serotonin uptake and inhibiting serotonin transporter? Is not it the same thing? How these transporters are being contacted? Can

these tansporters be isolated and used in in vitro studies? The examiner also does not agree with the applicants arguments regarding definiteness of clinical dysfunction.

In regard to prior art rejections over Meltzer's reference (J. Med. Chem.), the examiner does not agree with the applicants arguments that this reference can not be cited since it is applicant's own work. There are five additional inventors on this publication in addition to three common inventors and therefore, is available as a prior art reference since the invention was known to others. In regard to Zhao' reference, the applicants have amended claims to overcome this reference. However, this reference does constitute a prior art reference against newly submitted claims 46-49 as will be discussed later under new grounds of rejection. In regard to WO reference, the applicants have amended claims to overcome specific compounds 11, 20 and 21. However, this reference still anticipates the instant claims when R1 represents -COR3 and R2 represents -OH group in the compounds of formulae I, II and III (see pages 7-8 and claim 1). Similarly, both the U.S. patents still anticipate the instant claims when R1 represents -COR3 and R2 represents OH group in compounds of formulae I, II and III.

Conclusion

4. Rejection of claims 30, 31, 33-35, 37 and 39-43 under 35 U.S.C. 112, first paragraph is maintained for the reasons of record.
5. Rejection of claims 25-28, 30, 31 and 42 under 35 U.S.C. 112, second paragraph is maintained for the reasons of record.
6. All prior art rejections under 35 U.S.C. 102(a) and 102(e) are maintained for the reasons of record.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 9 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the value of variable X defined as C=CX1Y, with the N being member of the ring is indefinite since it is not clear whether only X1 (defined as NR3 or NSO2R3) is part of the ring or whole C=CX1Y is part of the ring.

Claim 9 recites the limitation "N for variable X" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

In claim 44, it is not clear what is being claimed ? Is it ----A compound having structural formula----? Also, the value of variable R9 defined as protecting group is indefinite. The applicants are suggested to include specific values.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 46-49 are rejected under 35 U.S.C. 102(a) as being anticipated by Meltzer (J. Med. Chem. Vol. 44, 2001, cited on applicants form 1449).

Meltzer discloses synthesis of 6- and 7-hydroxy-8-azabicyclo[3.2.1]octanes and their binding affinity for the dopamine and serotonin transporters. The compounds 19 and 20

(see scheme 2 on page 2621) disclosed by Meltzer clearly anticipate the instant claims.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 46-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao (J. Med., Chem. Cited on applicants form 1449).

Zhao discloses synthesis and pharmacology of 6- and 7-hydroxylated 2-carbomethoxy-3-(p-tolyl)tropanes. The compounds 16 (see scheme 3 on page 3286) and 28 (see scheme 5 on page 3287) disclosed by Zhao clearly anticipate the instant claims.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-7, 9-18, 20-28, 44 and 45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 21, 22, 27 and 32 of U.S. Patent No. 6,353,105. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are

encompassed by broader values of variables R1 and R2 in compounds of formulae I, II and III of the cited patent, specifically when R1 represents COR3 and R2 represents OH or OR3 group.

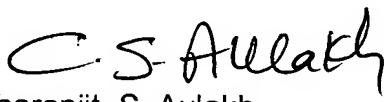
13. Claims 1-7, 9-18, 20-24, 29-31, 33-35, 37 and 39-45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-22 of U.S. Patent No. 6,670,375. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are encompassed by broader values of variables R1 and R2 in compounds of the cited patent, specifically when R1 represents COR3 and R2 represents OR3 group.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1625

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Charanjit S. Aulakh
Primary Examiner
Art Unit 1625